1. SCIENTIFIC ABSTRACT:

The long-term goal of our study is to develop effective immunotherapy for patients with ovarian cancer. Ovarian cancer and other cancers that spread to involve the peritoneal cavity are a significant cause of cancer related morbidity and mortality. The intraperitoneal delivery of chemotherapy and biological agents resulted in clinically significant responses in certain patients with peritoneal carcinomatosis, and particularly in those patients with small tumor burdens. T-cell immunity requires that at least 2 signaling pathways are activated, one through the TCR-CD3 complex and the other through the CD28 receptor. Ligands for these reactions are situated on the MHC antigen and costimulatory molecules respectively. These structures are coexpressed on competent antigen presenting cells such as dendritic cells and certain macrophages. Tumor cells may have impaired antigen presenting functions because of decreased expression of MHC antigens and/or absent expression of costimulatory molecules. The presence of the B7.1 surface molecule on immunizing tumor cells has been shown in preclinical studies to be an important factor in the induction of antitumor immunity. We have recently shown that the peritoneal dendritic cells from patients with ovarian carcinoma rarely express the B7.1 antigen, and B7.1 is not expressed on ovarian carcinoma cells. We and others have shown that the expression of HLA Class I and HLA Class II antigens can be increased on peritoneal carcinoma cells *in vivo* after IP injection of rIFN-γ. The proposed clinical trial will test the hypothesis that IP injections of autologous ovarian carcinoma cells that express B7.1 after infection with a canarypox vector (nonreplicating virus) that includes the gene for the B7.1 molecule (ALVAC B7.1 Pasteur Merieux, Connaught France), activates antitumor T-lymphocyte responses *in vivo*. Tumor cells will be pretreated with a low concentration of rIFN-γ *ex vivo* prior to infection with ALVAC B7.1. The specific objectives of this pilot clinical trial are to determine whether IP injections of a therapeutic vaccine, comprised of autologous ovarian cancer cells infected with ALVAC-hB7.1 (AUT-OV-ALVAC-hB7.1) in combination with IP rIFN-γ:

(1) Is feasible, and has acceptable clinical toxicity;

(2) Results in activation of tumor specific immunity *in vivo*, determined by: (i) autologous tumor cytotoxic lymphocyte (CTL) activity; (ii) autologous tumor induced T-lymphocyte proliferation and Th_1 type cytokine production.

(3) Results in an increase in the proportions of $CD3^+TCR\alpha\beta^+$ cells that express T-lymphocyte activation markers.

(4) Produces clinical responses (major or minor).